

# Bilateral Breast Masses as Initial Presentation of Widely Metastatic Melanoma

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**Background and Objectives:** Malignant melanoma is the most rapidly increasing cancer in the world. Metastatic disease occurs in 20% of patients. Metastatic cancer to the breast is rare, but primary breast cancer is one of the leading causes of death in women. In the present study, a large personal series of breast biopsies is reviewed, and 2 cases of metastatic malignant melanoma to both breasts are reported.

**Methods:** A personal series of 1,200 breast biopsies from 1975 to 1998 were reviewed. In this series, 2 cases of metastatic melanoma to both breasts were identified.

**Results:** Two female patients, ages 31 and 34 years, were evaluated for bilateral breast masses. Both were treated with simple excision of the breast tumor. Postoperatively, both patients were found to have widespread metastatic disease to the brain, lung, and liver. Despite aggressive treatment with chemotherapy and radiation, the patients died at 6 and 22 months, respectively, after the initial presentation.

**Conclusion:** Bilateral breast metastasis from malignant melanoma is rare. Care must be taken to make a correct diagnosis of metastatic melanoma rather than of primary breast cancer. An incorrect diagnosis of anaplastic carcinoma can lead to major surgical procedures that are of no value. The long-term prognosis of patients with bilateral breast metastasis from malignant melanoma is poor.

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**KEY WORDS:** metastatic malignant melanoma; breast metastasis

## INTRODUCTION

Malignant melanoma is one of the most rapidly increasing cancers in the world. The incidence of cutaneous malignant melanoma is expected to be 1 in 75 by the year 2000 [1]. Approximately 20% of patients will develop metastasis [2]. When metastases occur, the most common sites are liver, lung, and brain. Metastases to the breast from malignant melanoma or any other neoplasm is rare. In about 40% of patients with metastasis to the breast from an extramammary source, the breast lesion is the first manifestation of disease [3]. Although the incidence of metastatic melanoma and other cancers to the breast is rare, the exact recognition of this clinical problem is important. The correct management of metastatic disease to the breast can prevent unnecessary mutilation. In any premenopausal patient who has bilateral breast masses, the possibility of metastatic disease from malignant melanoma must be considered in the differential diagnosis.

## MATERIAL AND METHODS

From July 1975 to January 1999, >1,200 breast biopsies were performed. This series over 23 years included 1,154 women and 51 men. Three hundred twelve women and 7 men had a positive biopsy for cancer. In this series, 23 patients had bilateral breast biopsies at the same operative procedure. Of these 23 patients, 21 were female and 2 were male. Of the patients with bilateral breast biopsies at the same operative procedure, only 9 were positive for cancer, and all were female. Two patients in this group had a final pathology report of metastatic malignant melanoma after an initial frozen-section report of anaplastic carcinoma of the breast.

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The first patient was a 31-year-old Caucasian woman referred for evaluation of bilateral breast masses. Mammograms indicated the breast nodules to have benign characteristics. Needle aspiration of the masses indicated the tissue to be solid. Bilateral breast biopsies were initially diagnosed by the pathologist as anaplastic carcinoma of the breast. Additional history remembered by the patient after the breast biopsy revealed that she had a malignant melanoma removed from the right shoulder 4 years earlier. Further analysis of the breast biopsy slides with immunoperoxidase stains (S-100, positive; Cytokeratin, negative; HMB-45, positive) showed the tumor to be metastatic melanoma. The breast metastasis was identical to the primary melanoma when the original slides were obtained for comparison. The original tumor was a Clarks level IV and a thickness of 1.9 mm. All margins were clear from the original surgical excision. Of ancillary interest is the history of the death of the patient's mother in her mid-30s from widely metastatic melanoma.

Complete staging of the patient showed metastatic melanoma in the subcutaneous tissue of the right chest wall, 3 pulmonary nodules, several brain metastases to both cerebral hemispheres and the cerebellum, and a single metastasis located behind the uterus. The patient was treated with dacarbazine, cisplatin, velban, and interferon on the basis of chemosensitivity testing. The tissue was negative for hormone receptors, and consequently Tamoxifen was not prescribed. The brain was irradiated under the protection of dexamethasone. The patient received 3,000 cGy in 10 increments to the entire brain and cranial meninges.

Despite multiple courses of chemotherapy, stereotactic radiosurgery of the brain, and excision of the right middle lobe of the lung, the patient died 22 months after the initial diagnosis of stage IV widely disseminated malignant melanoma.

The second patient was a 34-year-old Caucasian woman referred for a wide excision of a previously biopsied Clarks level IV malignant melanoma of the left upper back, with a thickness of 2.2 mm. A wide excision was scheduled with an advancement flap for skin coverage.

During the preoperative history and physical examination, a small mass was palpated in the upper outer quadrants of each breast. Mammograms and ultrasound scans were interpreted as probable benign fibroadenoma. The wide excision of the melanoma with an advancement flap was completed at the same time as bilateral breast biopsies. The frozen-section breast biopsies showed anaplastic carcinoma. Immunoperoxidase stains with further pathologic evaluation showed both breast tumors to be identical to the primary melanoma of the back.

A complete work-up showed metastatic melanoma to the brain, liver, lung, and soft tissue of the left thigh. The patient received radiation to the brain and several cycles

of chemotherapy. She did not respond and died 6 months after the initial diagnosis of stage IV widely disseminated malignant melanoma.

## DISCUSSION

Primary cancer of the breast is a leading cause of death from malignant disease in women. Metastatic cancer to the breast gland is rare [3]. Malignant melanoma is currently one of the most rapidly increasing neoplasms in frequency in the world [1]. Melanomas and lymphomas are the most common source of metastases to the breast [4–6]. The incidence of metastasis to the breast ranges from 1.7% to 6.6% in old autopsies series [7,8]. Lower values of 1.2%–2% have been reported in several clinical reviews [4,5]. During a recent 10-year period, 4,000 cancers of the breast were diagnosed and treated at Memorial Sloan-Kettering Hospital, New York [4]. In this 10-year period, only 14 cases of melanoma metastatic to the breast were reported in the series, for an incidence of 0.3% [4]. Only 1 patient had bilateral breast metastatic [4]. The average age of patients with melanoma metastatic to the breast reported in several series was 38–40 years, and most were premenopausal [2,5]. The median interval from the diagnosis of the primary malignant melanoma and the finding of breast metastases has been reported to be 33 months [2,5], but 1 case was reported in which a breast metastases was found 11 years after the primary tumor was excised [2]. About 300 cases of metastatic cancer to the breast have been reported in the English-language literature, and most are included in relatively small series or single case reports [9]. Metastatic malignant melanoma has accounted for slightly <100 of these cases [10]. Bilateral breast metastasis from malignant melanoma has been reported in only 11 cases [2,5,8,10].

An autopsy series of patients with melanoma metastatic to the breast showed they were considerably younger (49.7 vs. 62.7 years) than patients with other tumors metastatic to the breast [10]. A clinical review of 15 patients with breast metastases from malignant melanoma had a median age of 38 years, and 14 of 15 were premenopausal [2]. In premenopausal patients with breast metastasis, the most common site of the primary melanoma was on the arms and trunk [2]. This is in contrast to the most common site for primary malignant melanoma in premenopausal women, which is usually on the lower extremities [2,11]. Patients with extremity primary lesions and who are premenopausal have a significantly better prognosis and less incidence of metastatic disease than postmenopausal women and all men [11]. A previous report in the literature has suggested that there may be a certain barrier against metastization of melanoma in premenopausal women [12]. After menopause, the sex of the patient has no further effect on the course of the disease [11]. After menopause, there appears to be equal occurrence of melanomas between the trunk and

extremities [1]. The predilection for metastatic spread to the breasts in premenopausal women may occur from direct lymphatic or vascular drainage, or hormonal influences may be involved in the translocation of the melanoma cell to the breast parenchyma. Estrogen receptors occasionally have been found on melanoma cell metastasis and, when found, are in low levels [13]. Metastatic melanomas to both breasts in both patients in this report were negative for estrogen and progesterone receptors. Breast metastases from melanoma may occur in younger women because of the greater vascularity of their breasts compared with that in older women. Metastatic melanoma to the breast frequently occurs as a solitary nodule in the upper outer quadrant, which has the most abundant glandular tissue and consequently the best blood supply [14].

Bilateral breast metastasis from malignant melanoma is always associated with widely disseminated disease. Both patients in this report had ancillary metastatic disease in the brain, lung, liver, and subcutaneous tissue. These sites of metastatic involvement are similar to those reported in other series [2,10]. Therefore, the finding of melanoma metastatic to the breast requires a complete evaluation for ancillary metastatic disease, especially in the brain. Both patients in this report died from sequelae from the metastatic intracranial tumors.

It is crucial to recognize that malignant breast tumors may be metastatic melanoma to prevent unnecessary surgery. The first patient in this report was being prepared for bilateral mastectomies when the history of a previously excised melanoma of the back was recalled by the patient and her family. Melanoma metastases to the breast are typically well circumscribed and dense [15]. Mammographically, the mass has slightly irregular margins, and there are no microcalcifications or secondary skin or nipple changes. These mammographic features can lead to a difficult differential diagnosis with benign breast lesions, such as a fibroadenoma [15]. It is universally accepted that an excisional biopsy is sufficient to control locally all metastatic tumors to the breast. Histologic diagnosis of metastatic melanoma may be difficult unless appropriate immunoperoxidase stains are used.

The overall prognosis of patients with malignant melanoma metastatic to the breast is poor, with an average survival from diagnosis to time of death of 10 months [2,9,10]. Despite aggressive therapy in both reported patients, their survivals were only 6 and 22 months from the

time of diagnosis, with death as a sequelae from metastasis to the brain.

In conclusion, malignant melanoma metastatic to both breasts is uncommon. Only 11 previously reported cases are present in the literature [2,4,5,10]. The clinical prognosis is poor, with usual survival of <1 year despite very aggressive radiation and chemotherapy. It is very important for the surgeon and pathologist to consider the diagnosis of metastatic malignant melanoma whenever an anaplastic tumor is found in a breast biopsy from a 20- to 40-year-old woman, especially if the finding is bilateral. The treatment of metastatic malignant melanoma to the breast is excision of the metastasis with clear margins and systemic chemotherapy for the primary disease. Extreme care is advocated in the treatment of these patients; an incorrect diagnosis can lead to major disfiguring surgical procedures that are of no benefit to a patient whose survival is usually <1 year.

## REFERENCES

1. Ahmed I: Malignant melanoma: prognostic indicators. *Mayo Clin Proc* 1997;72:356-361.
2. Arora R, Robinson WA: Breast metastases from malignant melanoma. *J Surg Oncol* 1992;50:27-29.
3. Hanna NN, O'Donnell K, Wolfe GRZ: Alveolar soft part sarcoma metastatic to the breast. *J Surg Oncol* 1996;61:159-162.
4. Hajdu SI, Urban JA: Cancers metastatic to the breast. *Cancer* 1972;29:1691-1696.
5. Toombs BD, Kalisher L: Metastatic disease to the breast: clinical, pathologic, and radiographic features. *AJR* 1977;129:673-676.
6. Pressman PI: Malignant melanoma and the breast. *Cancer* 1973;31:784-788.
7. Abrams HL, Spiro R, Goldstein N: Metastases in carcinoma: analysis of 2000 autopsied cases. *Cancer* 1950;3:74-85.
8. Sandison AT: Metastatic tumors in the breast. *Br J Surg* 1959;47:54-58.
9. Amichitti M, Perani B, Boi S: Metastases to the breast from extramammary malignancies. *Oncology* 1990;47:257-260.
10. DiBonito L, Luchi M, Giarelli L, et al.: Metastatic tumors to the female breast: an autopsy study of 12 cases. *Pathol Res Pract* 1991;187:342-436.
11. Shaw HM, McGovern VJ, Milton GW, et al.: Malignant melanoma: influence of site of lesion and age of patient in the female superiority in survival. *Cancer* 1980;46:2731-2735.
12. Olsen G: The malignant melanoma of the skin. *Acta Chir Scand* 1966;365(Suppl):1-222.
13. Lee YN: Better prognosis of many cancers in females. A phenomenon not explained by study of steroid receptors. *J Surg Oncol* 1984;25:255-262.
14. Vergier B, Trojani M, De Mascarel I: Metastases to the breast: differential diagnosis from primary breast carcinoma. *J Surg Oncol* 1991;48:112-116.
15. Bohman LG, Bassett LW, Gold RH, Voet R: Breast metastases from extramammary malignancies. *Radiology* 1982;144:309-312.
16. D'Orsi CJ, Feldhaus L, Sonnenfeld M: Unusual lesions of the breast. *Radiol Clin North Am* 1983;21:67-80.